Complete Summary

GUIDELINE TITLE

Haematuria.

BIBLIOGRAPHIC SOURCE(S)

Finnish Medical Society Duodecim. Haematuria. In: EBM Guidelines. Evidence-Based Medicine [Internet]. Helsinki, Finland: Wiley Interscience. John Wiley & Sons; 2008 Jun 3 [Various]. [16 references]

GUIDELINE STATUS

This is the current release of the guideline.

This guideline updates a previous version: Finnish Medical Society Duodecim. Haematuria. In: EBM Guidelines. Evidence-Based Medicine [Internet]. Helsinki, Finland: Wiley Interscience. John Wiley & Sons; 2004 Aug 26 [Various].

COMPLETE SUMMARY CONTENT

SCOPE

DISEASE/CONDITION(S)

Hematuria

GUIDELINE CATEGORY

Diagnosis
Evaluation

CLINICAL SPECIALTY

Family Practice
Internal Medicine
Nephrology
Oncology
Pediatrics
Urology

INTENDED USERS

Health Care Providers
Physicians

GUIDELINE OBJECTIVE(S)

Evidence-Based Medicine Guidelines collect, summarize, and update the core clinical knowledge essential in general practice. The guidelines also describe the scientific evidence underlying the given recommendations.

TARGET POPULATION

Patients with hematuria

INTERVENTIONS AND PRACTICES CONSIDERED

Diagnosis/Evaluation

1. Medical history
2. Clinical investigation
    - Physical examination
    - Laboratory tests
        - Urinalysis
        - Coagulation analysis
        - Tests for prostatic disease, immunoglobulin A nephropathy, systemic disease
        - Tests of renal function
        - Erythrocyte morphology
        - Cytology
    - Diagnostic tests in selected patients
        - Ultrasound of kidneys and urinary tract
        - Cystoscopy
        - Urography
        - Angiography
        - Pyelography
        - Computed tomography
        - Renal biopsy

MAJOR OUTCOMES CONSIDERED

Sensitivity and reliability of diagnostic tests

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Hand-searches of Published Literature (Primary Sources)
Hand-searches of Published Literature (Secondary Sources)
Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

The evidence reviewed was collected from the Cochrane database of systematic reviews and the Database of Abstracts of Reviews of Effectiveness (DARE). In addition, the Cochrane Library and medical journals were searched specifically for original publications.

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Classification of the Quality of Evidence

Code	Quality of Evidence	Definition
A	**High**	Further research is very unlikely to change our confidence in the estimate of effect. • Several high-quality studies with consistent results • In special cases: one large, high-quality multi-centre trial
B	**Moderate**	Further research is likely to have an important impact on confidence in the estimate of effect and may change the estimate. • One high-quality study • Several studies with some limitations
C	**Low**	Further research is very likely to have an important impact on confidence in the estimate of effect and is likely to change the estimate.

Code	Quality of Evidence	Definition
		• One or more studies with severe limitations
D	**Very Low**	Any estimate of effect is very uncertain. • Expert opinion • No direct research evidence • One or more studies with very severe limitations

GRADE (Grading of Recommendations Assessment, Development and Evaluation) Working Group 2007 (modified by the EBM Guidelines Editorial Team).

METHODS USED TO ANALYZE THE EVIDENCE

Systematic Review

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not stated

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Not stated

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Not applicable

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Not stated

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

The levels of evidence [A-D] supporting the recommendations are defined at the end of the "Major Recommendations" field.

Aims

- Exclude urinary tract infection and blood contamination (menstruation, sexual trauma, etc.)
- Further investigations should be carried out in all patients with confirmed haematuria that is not explained by the above causes (Carson, Segura, & Greene, 1979; Ritchie, Bevan, & Collier, 1986; Rockall et al., 1997; Benbassat et al., 1996) (Buntinx & Wauters, 1997) [**C**].

Macroscopic Haematuria

- Less than 0.5 mL of blood in 500 mL of urine causes macroscopic haematuria. Depending on the urine pH the colour of urine may vary from bright red to almost black. Usually the patient is correct when he/she has noticed the urine to be "bloody."
- Red coloured urine may also be caused by
    - Certain foods (beetroot)
    - Medication (nitrofurantoin, rifampicin)
    - Acute porphyria

Microscopic Haematuria

- More than three erythrocytes/high power field in sediment analysis
- More than five erythrocytes/0.9 mm^3 in counting chamber
- More than 15 X 10^6 erythrocytes/L in particle counting by flow cytometry

Investigations of Patients with Haematuria

- It should be noted that there is not necessarily a correlation between the degree of haematuria and the severity of the underlying disease. Thus, scant haematuria should be investigated as thoroughly as more significant haematuria.
- If a dipstick test is positive for blood, the finding must be confirmed with a fresh urine sample after a couple of days. The urine must also be examined microscopically. Confirmed haematuria is always an indication for further investigations (Cohen & Brown, 2003).
    1. Exclude urinary tract infection and contamination
    2. All patients
        - Thorough clinical investigation
        - Urinalysis: proteinuria, erythrocyte morphology, casts, leucocytes
            - If the erythrocyte morphology (acanthocytes or red-cell casts) in microscopic haematuria is suggestive of glomerular aetiology, and the patient has no proteinuria or renal impairment (creatinine normal), no further investigations are needed. However, the patient should be monitored with occasional checks (first follow-up at 6 months and annually thereafter) for the possible

development of proteinuria or renal impairment (Cohen & Brown, 2003).
    - Blood tests (see below)
    - Ultrasound examination of the kidneys and urinary tract
        - All patients if glomerular haematuria has not been verified with urinalysis or blood tests
    - Cytology (daytime sample) for patients over 40 years of age.

3. Cystoscopy
    - In patients over 50 years of age (Cohen & Brown, 2003); in younger patients only if haematuria has been macroscopic or the patient has risk factors for bladder cancer (smoking, occupational exposure, history of cyclophosphamide treatment)
    - Suspicious cells in cytology
    - Increased serum prostate specific antigen (PSA)
    - Ultrasound examination suggestive of bladder pathology

4. Other investigations for selected patients
    - Computed tomography (investigation of choice for suspected urinary calculi or tumour of the upper urinary tract)
    - Urography
    - Angiography
    - Pyelography
    - Renal biopsy

Medical History

- In what circumstances was haematuria noted (fever, physical activity, etc.)?
- Are there any other symptoms or signs (increased urinary frequency, dysuria, lower abdominal or flank pain)?
- Is haematuria seen at the initiation of, throughout, or at the end of voiding? Blood at the initiation suggests a urethral pathology, continuous haematuria a renal or ureteral problem, and blood at the end a bladder pathology.
- Are there any hereditary diseases or a tendency for urinary calculus formation?
- Travel abroad (exclude infectious diseases, such as schistosomiasis, malaria, etc.)
- Medication: use of nonsteroidal anti-inflammatory drugs (NSAIDs) or treatment with cytotoxic agents (cyclophosphamide)? These drugs may cause interstitial nephritis (NSAIDs), interstitial cystitis, or uroepithelial cancer (cytotoxic agents).

Clinical Investigation

- Look for petechiae, bruising or enlarged lymph nodes.
- Check blood pressure.
- Abdominal palpation (the size and contour of the liver, spleen, kidneys).
- Palpation of the prostate via the rectum.
- Laboratory tests should include coagulation analysis, tests for prostatic disease, immunoglobulin A (IgA) nephropathy, and tests for systemic disease and renal function (blood counts, erythrocyte sedimentation rate [ESR], C-reactive protein [CRP], creatinine, prostate specific antigen, possibly IgA).

Urinalysis

- Dipstick tests for blood are sensitive and reliable. False-positive results may be seen in
    - Haemoglobinuria
    - Myoglobinuria
- Reducing agents such as ascorbic acid reduce and even inhibit the staining reaction.
- A positive dipstick test must be confirmed by analysing the urine sediment (Bonnardeaux, Somerville, & Kaye, 1994).
    - A semiquantitative sediment analysis or quantitative counting chamber may be used. The semiquantitative sediment analysis is reliable in validated conditions.
    - The analysis is carried out on a fresh urine sample, voided before ingesting any fluid (an early morning sample). After the urine is centrifuged the sediment is analysed under a microscope using a 400x magnification.
    - The analysis offers much more information if the sediment is stained or analysed under a phase-contrast microscope. These methods enable observation on the shape of the erythrocytes, which in turn helps to localise the source of bleeding. Symmetric, round and normal appearing red blood cells (RBCs) are seen as a consequence of bleeding in the lower urinary tract, whereas dysmorphic red blood cells (acanthocytes) are seen in association with parenchymal renal disease ("glomerular bleeding") (Fairley & Birch, 1982; Schramek et al., 1989; Marcussen et al., 1992; van der Snoek et al., 1994).
- Culturing midstream urine and analysing urine sediment may not only confirm haematuria, but reveal an infection or the presence of leucocytes, casts, or abnormal cells. Abnormal cells are suggestive of a urinary tract malignancy. However, urinary cytology must always be included in the investigations.
- Sterile pyuria is typical not only of genitourinary tuberculosis, but is also seen in association with calculi and tumours. Concurrent proteinuria is usually suggestive of a renal parenchymal disease.
- Cellular, granular, fatty, or waxy casts in the sediment analysis are suggestive of a renal parenchymal disease.

Subsequent Investigations

- Ultrasound of the kidneys and, if necessary, urography
- Cytology of the urine
- Cystoscopy
- The importance of these investigations depends partly on the age of the patient. In children urography must be done only after careful consideration and cystoscopy is seldom necessary.
- Ultrasound investigation of the kidneys is safe and, particularly in pregnancy, the only recommended investigation. Sometimes additional investigations are needed, such as urography with tomography studies, computed tomography, angiography, and antegrade or retrograde pyelography.
- Urinary cytology: a random daytime sample is better than an early morning sample, but bladder wash cytology is the best. Generally three separate samples should be analysed for the highest diagnostic yield. Up to 80–90% of transitional cell bladder carcinomas may be diagnosed with urinary cytology

(Lewis et al., 1976; Sarnacki et al., 1971; Veltman et al., 1991; Morrison et al., 1984; Badalament et al., 1987).
- If the patient also has pyuria the urine should be cultured for tuberculosis.
- Cystoscopy is performed at the outpatient clinic under local anaesthesia.

Additional Investigations and Follow-up

- Possible additional investigations depend on the primary findings. The more investigations carried out the more likely it is that the underlying cause will be found. Urological investigations will reveal a cause in up to 80% of the cases (Carson, Segura, & Greene, 1979; Ritchie, Bevan, & Collier, 1986; Rockall et al., 1997).
- A renal biopsy will reveal a renal parenchymal disease. Renal biopsy should be considered particularly if the patient has simultaneous proteinuria, pathological casts, or dysmorphic erythrocytes suggestive of a glomerular haematuria. With this approach the patient may be saved from unnecessary antibiotic therapies, repeated radiographic investigations, or cystoscopies.
- Some causes of haematuria are listed in the table below, according to severity (serious causes indicate findings that necessitate major medical intervention or threaten the life of the patient).
- Haematuria in a young patient is usually caused by urinary tract infection, calculi, or parenchymal renal disease, particularly IgA nephropathy, whereas malignancy must be considered in patients over the age of 40 years (Ritchie, Bevan, & Collier, 1986). Therefore, haematuria must always be taken seriously.
- The cause of haematuria is not always revealed despite meticulous investigations. It may be necessary to follow up these patients, for example once a year, with a check-up of blood pressure and routine blood tests and urinalyses.

Table: Causes of Haematuria According to Severity

Serious	Moderate	Minor
• Renal carcinoma • Uroepithelial cancer • Ureteral stones • Prostate cancer • Hydronephrosis • Tuberculosis • Polycystic kidney disease • Parenchymal renal disease	• Kidney stones • Urinary tract infection • Interstitial cystitis • Bladder stones	• Asymptomatic prostatic hyperplasia

Related Resources

Refer to the original guideline document for related evidence, including Cochrane reviews and other evidence summaries.

Definitions:

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CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

REFERENCES SUPPORTING THE RECOMMENDATIONS

References open in a new window

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

Concise summaries of scientific evidence attached to the individual guidelines are the unique feature of the Evidence-Based Medicine Guidelines. The evidence summaries allow the clinician to judge how well-founded the treatment recommendations are. The type of supporting evidence is identified and graded for select recommendations (see the "Major Recommendations" field).

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Appropriate evaluation and diagnosis of hematuria

POTENTIAL HARMS

Although dipstick urinalysis tests for blood are sensitive and reliable, false-positive results may be seen in haemoglobinuria and myoglobinuria.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Getting Better

IOM DOMAIN

Effectiveness

IDENTIFYING INFORMATION AND AVAILABILITY

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ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2004 Aug 26 (revised 2008 Jun 3)

GUIDELINE DEVELOPER(S)

Finnish Medical Society Duodecim - Professional Association

SOURCE(S) OF FUNDING

Finnish Medical Society Duodecim

GUIDELINE COMMITTEE

Editorial Team of EBM Guidelines

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

Primary Author: Virpi Rauta

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Not stated

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GUIDELINE AVAILABILITY

This guideline is included in "EBM Guidelines. Evidence-Based Medicine" available from Duodecim Medical Publications, Ltd, PO Box 713, 00101 Helsinki, Finland; e-mail: info@ebm-guidelines.com; Web site: www.ebm-guidelines.com.

AVAILABILITY OF COMPANION DOCUMENTS

None available

PATIENT RESOURCES

None available

NGC STATUS

This NGC summary was completed by ECRI on August 29, 2005. This NGC summary was updated by ECRI Institute on September 29, 2008.

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